

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

**(19) World Intellectual Property
Organization
International Bureau**



(43) International Publication Date
23 December 2004 (23.12.2004)

PCT

(10) International Publication Number
WO 2004/110974 A1

(51) International Patent Classification⁷: C07C 59/48,
59/52, 59/56, 59/58, 59/68, 59/86, 233/33, 255/57, 291/14,
321/26, 323/33

(21) International Application Number:
PCT/EP2004/005966

(22) International Filing Date: 1 June 2004 (01.06.2004)

(25) Filing Language: English

(26) **Publication Language:** English

(30) **Priority Data:**
0312654.7 3 June 2003 (03.06.2003) GB

(71) **Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB];** Glaxo Wellcome House, Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).

(72) Inventors: and

(75) **Inventors/Applicants (for US only):** **GAINES, Simon** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **HOLMES, Ian, Peter** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **WATSON, Stephen, Paul** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB).

(74) **Agent: GIDDINGS, Peter, John; GlaxoSmithKline, Corporate Intellectual Property (CN925.1), 980 Great West Road, Brentford Middlesex TW8 9GS (GB).**

(81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

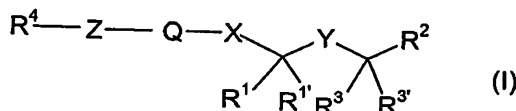
(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MATRIX METALLOPROTEINASE INHIBITORS



CO₂ R⁸, CONR⁵OR⁹ or NR⁵ COR¹⁰; R⁴ represents optionally substituted 5- or 6-membered aryl or heteroaryl; R⁵ represents H or C₁₋₃ alkyl; R⁶ and R⁷ each independently represents H, C₁₋₃ alkyl or halo; R⁸ represents H or C₁₋₂ alkyl; R⁹ represents H or C₁₋₃ alkyl; R¹⁰ and R¹¹ each independently represents H, C₁₋₆ alkyl or C₁₋₄ alkylaryl; and physiologically functional derivatives thereof, processes for their preparation, pharmaceutical formulations containing them and their use as inhibitors of matrix metal loproteinase enzymes (MMPs) are described.

(57) Abstract: Compounds of formula (1): Wherein: Q represents an optionally substituted 5- or 6-membered aryl or heteroaryl ring; X represents O, S, NR⁵ or CR⁶; R⁷; Y represents CHOH, CHSH, NOR⁸, CNR⁸ or CNOR⁸; Z represents a bond, CR¹⁰, R¹¹, O, S, SO, SO₂, NR¹⁰, OCR¹⁰, R¹¹, CR¹⁰, R¹¹O or Z, R⁴ and Q together form an optionally substituted fused tricyclic group; R¹, R^{1'}, R³ and R^{3'} each independently represents H, C₁₋₆ alkyl or C₁₋₄ alkylaryl; R² represents substituted 5- or 6-membered aryl or heteroaryl; R⁵ represents H or C₁₋₃ halo; R⁸ represents H or C₁₋₂ alkyl; R⁹ represents H or C₁₋₃ alkyl; R¹⁰ alkylaryl; and physiologically functional derivatives thereof, processes them and their use as inhibitors of matrix metal loproteinase enzymes

WO 2004/110974 A1